PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
SCB 873 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/011161	06.10.2004	09.10.2003
International Patent Classification (IPC) or national classification and IPC		
A61K38/17, C07K14/82		
Applicant		
INDENA S.P.A.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.07.2005	11.01.2006
Name and mailing address of the international preliminary examining authority:	Authorized Officer
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/011161

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-23 as originally filed

   Sequence listings part of the description, Pages

   1-22 as originally filed

   Claims, Numbers

   1-13 as originally filed

   Drawings, Sheets

   1/14-14/14 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Ad Section IV: Lack of unity of invention

The present application does not comply with the requirement of unity as set forth in Art. 34(3) and Rule 13 PCT.

An international application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same special technical features, special technical features being such features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Claim 1 is directed to a DNA transfer vector containing any one of 14 listed DNA sequences.

The technical relationship linking together the different nucleotide sequences (SEQ ID NO: 1-14) can be seen in the fact that they are all encode at least part of the human $p185^{neu}$ protein. As this protein is widely known in the state of the art, this relationship can not be considered novel or inventive. Thus, it cannot be accepted to constitute a special technical feature as defined above as it does not define a contribution which each of the different claimed inventions, considered as a whole, makes over the prior art.

Thus, the presently claimed subject-matter falls apart in 14 groups of inventions which are not unitarian, each group consisting of claims 1-13 with respect to each individual nucleic acid sequence.

As search and examination of the present application could be carried out without undue effort, it was chosen not to invite the applicant to restrict or pay additional examination fees.

Ad Section V: Reasoned statement with regard to novelty, inventive step or

industrial applicability

1) Documents

D1...Chen et al. (1998) Cancer Research 58: 1965-1971
D2...Amici et al. (2000) Gene Therapy 7: 703-706

2) Novelty

The present application relates to a DNA vaccines for the prevention or treatment of tumours expressing oncogenes of the ErbB family. The vectors of the present application contain DNA encoding the extracellular domain and the transmembrane domain of human $p185^{neu}$ wherein the extracellular domain may be truncated or replaced by corresponding fragments of the extracellular domain of rat $p185^{neu}$.

As the sequences as listed in SEQ ID NO: 1-14 have not been disclosed in the prior art as such, the subject-matter of **claims 1-13** is considered to meet the requirements of Art. 33(2) PCT.

3) Inventive step

The claims, however, do not meet the requirements of Art. 33(3) PCT as the claimed subject-matter does not involve an inventive step.

Constructs containing the extracellular and transmembrane domains of $p185^{neu}$ both from rat and human have been shown to be suitable for DNA vaccination for preventing or treating tumours (see, e.g, D1 or D2).

The difference between the constructs of the prior art and those claimed in claim 1 seems to lie in the fact that part of each construct is derived from the sequence coding for rat $p185^{neu}$.

The problem to be solved can be seen in the provision of DNA transfer vectors which

encode chimeric p185^{neu} which enhance the immune response in a patient.

This problem seems to be solved by some constructs as described in the examples and which correspond to Fig. 10-14. For such subject-matter an inventive step could in theory be acknowledged.

The claims, however, are directed to a number of sequences which certainly do not correspond to these constructs of Fig. 10-14 (SEQ ID NO: 1-9). As it is not clear that these constructs actually solve the above indicated problem an inventive step cannot be acknowledged for the current set of claims. It should further be noted that there is no evidence that SEQ ID NO: 10-14 actually do correspond to the plasmid constructs of Fig. 10-14.

Claims 1, 7, 10 and 12 as well as the claims dependent thereon are thus objected to under Art. 33(3) PCT.

Furthermore, **claim 10** is not clear. The wording "combined pharmaceutical preparation" in combination with the terms "sequential or separate therapeutic use" seems to be contradictory. The scope of the claim is thus not clear (Art. 6) PCT.